LDL Uptake by LDLR and TFR Pathways

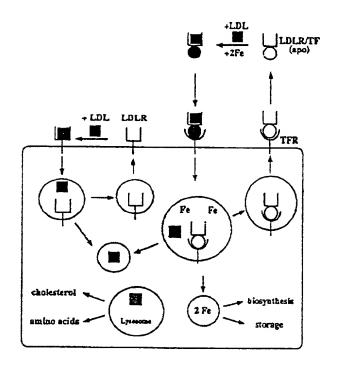
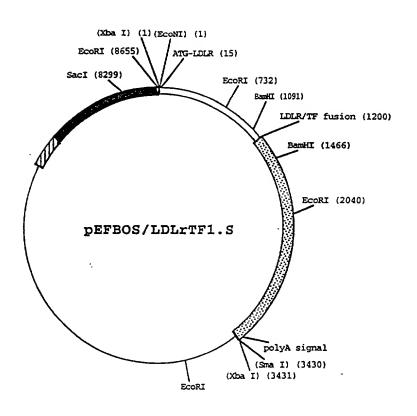




FIGURE 1



Legend:

SV 40 genomic sequences (position # 5092-160)

LDLR-cDNA sequence

EF-1α

Transferrin -cDNA sequence — puc 119

FIGURE 2 ,

Sea id no! 9

1 AGAGGCTGCGAGC ATG GGG CCC TGG GGC TGG AAA TTG CGC TGG ACC

1 Met Gly Pro Trp Gly Trp Lys Leu Arg Trp Thr

47 GTC GCC TTG CTC CTC GCC GCG GCG GGG ACT GCA GTG GGC GAC AGA 12 Val Ala Leu Leu Ala Ala Ala Gly Thr Ala Val Gly Asp Arg

92 TGT GAA AGA AAC GAG TTC CAG TGC CAA GAC GGG AAA TGC ATC TCC 27 Cys Giu Arg Asn Giu Phe Gin Cys Gin Asp Giy Lys Cys lie Ser

137 TAC AAG TGG GTC TGC GAT GGC AGC GCT GAG TGC CAG GAT GGC TCT 42 Tyr Lys Trp Vai Cys Asp Gly Ser Ala Glu Cys Gln Asp Gly Ser

182 GAT GAG TCC.CAG GAG ACG TGC TTG TCT GTC ACC TGC AAA TCC GGG 57 Asp Glu Ser Gin Glu Thr Cys Leu Ser Val Thr Cys Lys Ser Gly

227 GAC TTC AGC TGT GGG GGC CGT GTC AAC CGC TGC ATT CCT CAG TTC 72 Asp Phe Ser Cys Gly Gly Arg Val Asn Arg Cys lie Pro Gin Phe

272 TGG AGG TGC GAT GGC CAA GTG GAC TGC GAC AAC GGC TCA GAC GAG 87 Trp Arg Cys Asp Gly Gin Val Asp Cys Asp Asn Gly Ser Asp Glu

317 CAA GGC TGT CCC CCC AAG ACG TGC TCC CAG GAC GAG TTT CGC TGC 102 Gin Giy Cys Pro Pro Lys Thr Cys Ser Gin Asp Giu Phe Arg Cys

362 CAC GAT GGG AAG TGC ATC TCT CGG CAG TTC GTC TGT GAC TCA GAC 117 His Asp Gly Lys Cys IIe Ser Arg Gin Phe Val Cys Asp Ser Asp

407 CGG GAC TGC TTG GAC GGC TCA GAC GAG GCC TCC TGC CCG GTG CTC 132 Arg Asp Cys Leu Asp Gly Ser Asp Glu Ala Ser Cys Pro Val Leu

452 ACC TGT GGT CCC GCC AGC TTC CAG TGC AAC AGC TCC ACC TGC ATC 147 Thr Cys Gly Pro Ala Ser Phe Gln Cys Asn Ser Ser Thr Cys lle

497 CCC CAG CTG TGG GCC TGC GAC AAC GAC CCC GAC TGC GAA GAT GGC 162▶Pro Gin Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly

542 TCG GAT GAG TGG CCG CAG CGC TGT AGG GGT CTT TAC GTG TTC CAA 177 Ser Asp Glu Trp Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln

587 GGG GAC AGT AGC CCC TGC TCG GCC TTC GAG TTC CAC TGC CTA AGT 192 GIV Asp Ser Ser Pro Cys Ser Ala Phe Glu Phe His Cys Leu Ser

632 GGC GAG TGC ATC CAC TCC AGC TGG CGC TGT GAT GGT GGC CCC GAC 207 Gly Glu Cys ile His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp

677 TGC AAG GAC AAA TCT GAC GAG GAA AAC TGC GCT GTG GCC ACC TGT 222 Cys Lys Asp Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys

722 CGC CCT GAC GAA TTC CAG TGC TCT GAT GGA AAC TGC ATC CAT GGC 237 Arg Pro Asp Glu Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly 767 AGC CGG CAG TGT GAC CGG GAA TAT GAC TGC AAG GAC ATG AGC GAT 252 Ser Arg Gin Cys Asp Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp 812 GAA GTT GGC TGC GTT AAT GTG ACA CTC TGC GAG GGA CCC AAC AAG 267 FGIU Val Gly Cys Val Asn Val Thr Leu Cys Glu Gly Pro Asn Lys 857 TTC AAG TGT CAC AGC GGC GAA TGC ATC ACC CTG GAC AAA GTC TGC 282 Phe Lys Cys His Ser Gly Glu Cys IIe Thr Leu Asp Lys Val Cys 902 AAC ATG GCT AGA GAC TGC CGG GAC TGG TCA GAT GAA CCC ATC AAA 297▶Asn Met Ala Arg Asp Cys Arg Asp Trp Ser Asp Glu Pro lie Lys 947 GAG TGC GGG ACC AAC GAA TGC TTG GAC AAC AAC GGC GGC TGT TCC 312 FGlu Cys Gly Thr Asn Glu Cys Leu Asp Asn Asn Gly Gly Cys Ser 992 CAC GTC TGC AAT GAC CTT AAG ATC GGC TAC GAG TGC CTG TGC CCC 327 His Val Cys Asn Asp Leu Lys Ile Gly Tyr Glu Cys Leu Cys Pro 1037 GAC GGC TTC CAG CTG GTG GCC CAG CGA AGA TGC GAA GAT ATC GAT 342 Asp Gly Phe Gin Leu Val Ala Gln Arg Arg Cys Glu Asp Ile Asp 1082 GAG TGT CAG GAT CCC GAC ACC TGC AGC CAG CTC TGC GTG AAC CTG 357 FGlu Cys Gin Asp Pro Asp Thr Cys Ser Gin Leu Cys Val Asn Leu 1127 GAG GGT GGC TAC AAG TGC CAG TGT GAG GAA GGC TTC CAG CTG GAC 372 Glu Gly Gly Tyr Lys Cys Gln Cys Glu Glu Gly Phe Gln Leu Asp 1172 CCC CAC ACG AAG GCC TGC AAG GCT GTG GTC CCT GAT AAA ACT GTG 387 Pro His Thr Lys Ala Cys Lys Ala Val Val Pro Asp Lys Thr Val 1217 AGA TGG TGT GCA GTG TCG GAG CAT GAG GCC ACT AAG TGC CAG AGT 402 Arg Trp Cys Ala Val Ser Glu His Glu Ala Thr Lys Cys Gin Ser 1262 TTC CGC GAC CAT ATG AAA AGC GTC ATT CCA TCC GAT GGT CCC AGT 417 Phe Arg Asp His Met Lys Ser Val lie Pro Ser Asp Gly Pro Ser 1307 GTT GCT TGT GTG AAG AAA GCC TCC TAC CTT GAT TGC ATC AGG GCC 432 Val Ala Cys Val Lys Lys Ala Ser Tyr Leu Asp Cys Ile Arg Ala 1352 ATT GCG GCA AAC GAA GCG GAT GCT GTG ACA CTG GAT GCA GGT TTG 447 lie Ala Ala Asn Glu Ala Asp Ala Val Thr Leu Asp Ala Gly Leu 1397 GTG TAT GAT GCT TAC TTG GCT CCC AAT AAC CTG AAG CCT GTG GTG 462 Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu Lys Pro Val Val 1442 GCA GAG TTC TAT GGG TCA AAA GAG GAT CCA CAG ACT TTC TAT TAT 477 Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr Phe Tyr Tyr

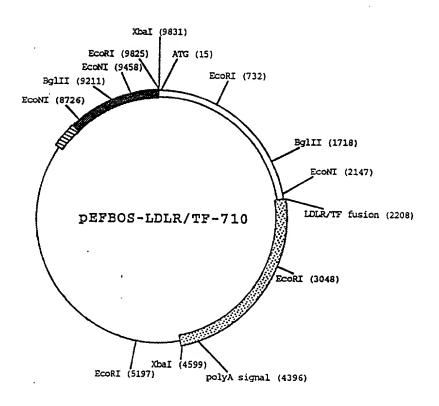
FIGURE 3B

1487 GCT GTT GCT GTG GTG AAG AAG GAT AGT GGC TTC CAG ATG AAC CAG 492 Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gin Met Asn Gin 1532 CTT CGA GGC AAG AAG TCC TGC CAC ACG GGT CTA GGC AGG TCC GCT 507 Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser Ala 1577 GGG TGG AAC ATC CCC ATA GGC TTA CTT TAC TGT GAC TTA CCT GAG 522 Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu 1622 CCA CGT AAA CCT CTT GAG AAA GCA GTG GCC AAT TTC TTC TCG GGC 537≯Pro Arg Lys Pro Leu Glu Lys Ala Val Ala Asn Phe Phe Ser Gly 1667 AGC TGT GCC CCT TGT GCG GAT GGG ACG GAC TTC CCC CAG CTG TGT 552 Ser Cys Ala Pro Cys Ala Asp Gly Thr Asp Phe Pro Gln Leu Cys 1712 CAA CTG TGT CCA GGG TGT GGC TGC TCC ACC CTT AAC CAA TAC TTC 567 Gin Leu Cys Pro Gly Cys Gly Cys Ser Thr Leu Asn Gin Tyr Phe 1757 GGC TAC TCG GGA GCC TTC AAG TGT CTG AAG GAT GGT GCT GGG GAT 582 Gly Tyr Ser Gly Ala Phe Lys Cys Leu Lys Asp Gly Ala Gly Asp 1802 GTG GCC TTT GTC AAG CAC TCG ACT ATA TTT GAG AAC TTG GCA AAC 597 Val Ala Phe Val Lys His Ser Thr lie Phe Glu Asn Leu Ala Asn 1847 AAG GCT GAC AGG GAC CAG TAT GAG CTG CTT TGC CTA GAC AAC ACC 612 Lys Ala Asp Arg Asp Gin Tyr Glu Leu Leu Cys Leu Asp Asn Thr 1892 CGG AAG CCG GTA GAT GAA TAC AAG GAC TGC CAC TTG GCC CAG GTC 627 Arg Lys Pro Val Asp Glu Tyr Lys Asp Cys His Leu Ala Gin Val 1937 CCT TCT CAT ACC GTC GTG GCC CGA AGT ATG GGC GGC AAG GAC GAC 642 Pro Ser His Thr Val Val Ala Arg Ser Met Gly Gly Lys Glu Asp 1982 TTG ATC TGG GAG CTT CTC AAC CAG GCC CAG GAA CAT TTT GGC AAA 657 Leu lle Trp Glu Leu Leu Asn Gin Ala Gin Glu His Phe Gly Lys 2027 GAC AAA TCA AAA GAA TTC CAA CTA TTC AGC TCT CCT CAT GGG AAG 672 Asp Lys Ser Lys Glu Phe Gln Leu Phe Ser Ser Pro His Gly Lys 2072 GAC CTG CTG TTT AAG GAC TCT GCC CAC GGG TTT TTA AAA GTC CCC 687 Asp Leu Leu Phe Lys Asp Ser Ala His Gly Phe Leu Lys Val Pro 2117 CCA AGG ATG GAT GCC AAG ATG TAC CTG GGC TAT GAG TAT GTC ACT 702 Pro Arg Met Asp Ala Lys Met Tyr Leu Gly Tyr Glu Tyr Val Thr 2162 GCC ATC CGG AAT CTA CGG GAA GGC ACA TGC CCA GAA GCC CCA ACA 717 Ala lie Arg Asn Leu Arg Glu Gly Thr Cys Pro Glu Ala Pro Thr 2207 GAT GAA TGC AAG CCT GTG AAG TGG TGT GCG CTG AGC CAC CAC GAG 732 Asp Glu Cys Lys Pro Val Lys Trp Cys Ala Leu Ser His His Glu

2252 AGG CTC AAG TGT GAT GAG TGG AGT GTT AAC AGT GTA GGG AAA ATA 747 Arg Leu Lys Cys Asp Glu Trp Ser Val Asn Ser Val Gly Lys ile 2297 GAG TGT GTA TCA GCA GAG ACC ACC GAA GAC TGC ATC GCC AAG ATC 762 GIU Cys Val Ser Ala Glu Thr Thr Giu Asp Cys lie Ala Lys lie 2342 ATG AAT GGA GAA GCT GAT GCC ATG AGC TTG GAT GGA GGG TTT GTC 777 Met Asn Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly Phe Vai 2387 TAC ATA GCG GGC AAG TGT GGT CTG GTG CCT GTC TTG GCA GAA AAC 792 Tyr lie Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala Glu Asn 2432 TAC AAT AAG AGC GAT AAT TGT GAG GAT ACA CCA GAG GCA GGG TAT 807 Tyr Asn Lys Ser Asp Asn Cys Glu Asp Thr Pro Glu Ala Gly Tyr 2477 TTT GCT GTA GCA GTG GTG AAG AAA TCA GCT TCT GAC CTC ACC TGG 822 Phe Ala Val Ala Val Val Lys Lys Ser Ala Ser Asp Leu Thr Trp 2522 GAC AAT CTG AAA GGC AAG AAG TCC TGC CAT ACG GCA GTT GGC AGA 837 Asp Asn Leu Lys Gly Lys Lys Ser Cys His Thr Ala Val Gly Arg 2567 ACC GCT GGC TGG AAC ATC CCC ATG GGC CTG CTC TAC AAT AAG ATC 852 Thr Ala Gly Trp Asn Ile Pro Met Gly Leu Leu Tyr Asn Lys Ile 2612 AAC CAC TGC AGA TTT GAT GAA TTT TTC AGT GAA GGT TGT GCC CCT 867 Asn His Cys Arg Phe Asp Glu Phe Phe Ser Glu Gly Cys Ala Pro 2657 GGG TCT AAG AAA GAC TCC AGT CTC TGT AAG CTG TGT ATG GGC TCA 882 Giy Ser Lys Lys Asp Ser Ser Leu Cys Lys Leu Cys Met Giy Ser 2702 GGC CTA AAC CTG TGT GAA CCC AAC AAA GAG GGA TAC TAC GGC 897 Gly Leu Asn Leu Cys Glu Pro Asn Asn Lys Glu Gly Tyr Tyr Gly 2747 TAC ACA GGC GCT TTC AGG TGT CTG GTT GAG AAG GGA GAT GTG GCC 912 Tyr Thr Gly Ala Phe Arg Cys Leu Val Glu Lys Gly Asp Val Ala 2792 TTT GTG AAA CAC CAG ACT GTC CCA CAG AAC ACT GGG GGA AAA AAC 927 Phe Val Lys His Gln Thr Val Pro Gln Asn Thr Gly Gly Lys Asn 2837 CCT GAT CCA TGG GCT AAG AAT CTG AAT GAA AAA GAC TAT GAG TTG 942 Pro Asp Pro Trp Ala Lys Asn Leu Asn Glu Lys Asp Tyr Glu Leu 2882 CTG TGC CTT GAT GGT ACC AGG AAA CCT GTG GAG GAG TAT GCG AAC 957 Leu Cys Leu Asp Gly Thr Arg Lys Pro Val Glu Glu Tyr Ala Asn 2927 TGC CAC CTG GCC AGA GCC CCG AAT CAC GCT GTG GTC ACA CGG AAA 972 Cvs His Leu Ala Arg Ala Pro Asn His Ala Val Val Thr Arg Lys 2972 <u>GAT AAG GAA GCT TGC GTC CAC AAG ATA TTA CGT CAA CAG CAC CAC</u> 987 Asp Lys Glu Ala Cys Val His Lys IIe Leu Arg Gln Gln Gln His

FIGURE 3D

FIGURE 3E



Legend:

SV 40 genomic sequences (position # 5092-160) ____ LDLR-cDNA sequence EF-1α Transferrin-cDNA sequence ____ puC 119

FIGURE 4

1 AGAGGCTGCGAGC ATG GGG CCC TGG GGC TGG AAA TTG CGC TGG ACC

1 Met Gly Pro Trp Gly Trp Lys Leu Arg Trp Thr

47 GTC GCC TTG CTC CTC GCC GCG GCG GGG ACT GCA GTG GGC GAC AGA 12 Val Ala Leu Leu Leu Ala Ala Gly Thr Ala Val Gly Asp Arg

92 TGT GAA AGA AAC GAG TTC CAG TGC CAA GAC GGG AAA TGC ATC TCC 27 Cys Glu Arg Asn Glu Phe Gin Cys Gin Asp Gly Lys Cys IIe Ser

137 TAC AAG TGG GTC TGC GAT GGC AGC GCT GAG TGC CAG GAT GGC TCT 42 Tyr Lys Trp Vai Cys Asp Gly Ser Ala Glu Cys Gln Asp Gly Ser

182 GAT GAG TCC CAG GAG ACG TGC TTG TCT GTC ACC TGC AAA TCC GGG 57 Asp Glu Ser Gln Glu Thr Cys Leu Ser Val Thr Cys Lys Ser Gly

227 GAC TTC AGC TGT GGG GGC CGT GTC AAC CGC TGC ATT CCT CAG TTC 72 Asp Phe Ser Cys Gly Gly Arg Val Asn Arg Cys !!e Pro Gin Phe

272 TGG AGG TGC GAT GGC CAA GTG GAC TGC GAC AAC GGC TCA GAC GAG 87 Trp Arg Cys Asp Gly Gin Val Asp Cys Asp Asn Gly Ser Asp Glu

317 CAA GGC TGT CCC CCC AAG ACG TGC TCC CAG GAC GAG TTT CGC TGC 102 Gin Gly Cys Pro Pro Lys Thr Cys Ser Gin Asp Glu Phe Arg Cys

362 CAC GAT GGG AAG TGC ATC TCT CGG CAG TTC GTC TGT GAC TCA GAC 117 His Asp Gly Lys Cys IIe Ser Arg Gin Phe Vai Cys Asp Ser Asp

407 CGG GAC TGC TTG GAC GGC TCA GAC GAG GCC TCC TGC CCG GTG CTC 132 Arg Asp Cys Leu Asp Gly Ser Asp Glu Ala Ser Cys Pro Val Leu

452 ACC TGT GGT CCC GCC AGC TTC CAG TGC AAC AGC TCC ACC TGC ATC 147 Thr Cys Giy Pro Aia Ser Phe Gin Cys Asn Ser Ser Thr Cys iie

497 CCC CAG CTG TGG GCC TGC GAC AAC GAC CCC GAC TGC GAA GAT GGC 162 Pro Gin Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly

542 TCG GAT GAG TGG CCG CAG CGC TGT AGG GGT CTT TAC GTG TTC CAA 177 Ser Asp Giu Trp Pro Gin Arg Cys Arg Gly Leu Tyr Val Phe Gin

587 GGG GAC AGT AGC CCC TGC TCG GCC TTC GAG TTC CAC TGC CTA AGT 192 GIV Asp Ser Ser Pro Cys Ser Ala Phe Glu Phe His Cys Leu Ser

632 GGC GAG TGC ATC CAC TCC AGC TGG CGC TGT GAT GGT GGC CCC GAC 207 Gly Gly Cys lie His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp

677 TGC AAG GAC AAA TCT GAC GAG GAA AAC TGC GCT GTG GCC ACC TGT 222 Cys Lys Asp Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys

FIGURE 5A

722 CGC CCT GAC GAA TTC CAG TGC TCT GAT GGA AAC TGC ATC CAT GGC 237 Arg Pro Asp Glu Phe Gin Cys Ser Asp Gly Asn Cys ile His Gly 767 AGC CGG CAG TGT GAC CGG GAA TAT GAC TGC AAG GAC ATG AGC GAT 252 Ser Arg Gin Cys Asp Arg Giu Tyr Asp Cys Lys Asp Met Ser Asp 812 GAA GTT GGC TGC GTT AAT GTG ACA CTC TGC GAG GGA CCC AAC AAG 267 Glu Val Gly Cys Val Asn Val Thr Leu Cys Glu Gly Pro Asn Lys 857 TTC AAG TGT CAC AGC GGC GAA TGC ATC ACC CTG GAC AAA GTC TGC 282 Phe Lys Cys His Ser Gly Glu Cys IIe Thr Leu Asp Lys Val Cys 902 AAC ATG GCT AGA GAC TGC CGG GAC TGG TCA GAT GAA CCC ATC AAA 297 Asn Met Ala Arg Asp Cys Arg Asp Trp Ser Asp Glu Pro IIe Lys 947 GAG TGC GGG ACC AAC GAA TGC TTG GAC AAC AAC GGC GGC TGT TCC 312 Glu Cys Gly Thr Asn Glu Cys Leu Asp Asn Asn Gly Gly Cys Ser 992 CAC GTC TGC AAT GAC CTT AAG ATC GGC TAC GAG TGC CTG TGC CCC 327 His Val Cys Asn Asp Leu Lys lle Gly Tyr Glu Cys Leu Cys Pro 1037 GAC GGC TTC CAG CTG GTG GCC CAG CGA AGA TGC GAA GAT ATC GAT 342 Asp Gly Phe Gin Leu Val Ala Gin Arg Arg Cys Glu Asp lle Asp 1082 GAG TGT CAG GAT CCC GAC ACC TGC AGC CAG CTC TGC GTG AAC CTG 357 FGiu Cys Gin Asp Pro Asp Thr Cys Ser Gin Leu Cys Val Asn Leu 1127 GAG GGT GGC TAC AAG TGC CAG TGT GAG GAA GGC TTC CAG CTG GAC 372 Glu Gly Gly Tyr Lys Cys Gin Cys Glu Glu Gly Phe Gin Leu Asp 1172 CCC CAC ACG AAG GCC TGC AAG GCT GTG GGC TCC ATC GCC TAC CTC 387 Pro His Thr Lys Ala Cys Lys Ala Val Gly Ser Ile Ala Tyr Leu 1217 TTC TTC ACC AAC CGG CAC GAG GTC AGG AAG ATG ACG CTG GAC CGG 402) Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg 1262 AGC GAG TAC ACC AGC CTC ATC CCC AAC CTG AGG AAC GTG GTC GCT 417 Ser Glu Tyr Thr Ser Leu IIe Pro Asn Leu Arg Asn Val Val Ala 1307 CTG GAC ACG GAG GTG GCC AGC AAT AGA ATC TAC TGG TCT GAC CTG 432 Leu Asp Thr Giu Val Ala Ser Asn Arg lie Tyr Trp Ser Asp Leu 1352 TCC CAG AGA ATG ATC TGC AGC ACC CAG CTT GAC AGA GCC CAC GGC 447 Ser Gin Arg Met lie Cys Ser Thr Gin Leu Asp Arg Ala His Gly 1397 GTC TCT TCC TAT GAC ACC GTC ATC AGC AGG GAC ATC CAG GCC CCC 462 Val Ser Ser Tyr Asp Thr Val lie Ser Arg Asp lie Gin Ala Pro 1442 GAC GGG CTG GCT GTG GAC TGG ATC CAC AGC AAC ATC TAC TGG ACC 477 Asp Gly Leu Ala Val Asp Trp lle His Ser Asn lle Tyr Trp Thr

FIGURE 5B

1487 GAC TCT GTC CTV GGC ACT GTC TCT GTT GCG GAT ACC AAG GGC GTG 492 Asp Ser Val Leu Gly Thr Val Ser Val Ala Asp Thr Lys Gly Val 1532 AAG AGG AAA ACG TTA TTC AGG GAG AAC GGC TCC AAG CCA AGG GCC 507 Lys Arg Lys Thr Leu Phe Arg Glu Asn Gly Ser Lys Pro Arg Ala 1577 ATC GTG GTG GAT CCT GTT CAT GGC TTC ATG TAC TGG ACT GAC TGG 522 lie Val Val Asp Pro Val His Gly Phe Met Tyr Trp Thr Asp Trp 1622 GGA ACT CCC GCC AAG ATC AAG AAA GGG GGC CTG AAT GGT GTG GAC 537 FGIY Thr Pro Ala Lys IIe Lys Lys GIY GIY Leu Asn GIY Val Asp 1667 ATC TAC TCG CTG GTG ACT GAA AAC ATT CAG TGG CCC AAT GGC ATC 552≯lle Tyr Ser Leu Val Thr Giu Asn lle Gin Trp Pro Asn Giy lle 1712 ACC CTA GAT CTC CTC AGT GGC CGC CTC TAC TGG GTT GAC TCC AAA 567 Thr Leu Asp Leu Leu Ser Gly Arg Leu Tyr Trp Val Asp Ser Lys 1757 CTT CAC TCC ATC TCA AGC ATC GAT GTC AAT GGG GGC AAC CGG AAG 582 Leu His Ser lie Ser Ser lie Asp Val Asn Gly Gly Asn Arg Lys 1802 ACC ATC TTG GAG GAT GAA AAG AGG CTG GCC CAC CCC TTC TCC TTG 597 Thr lie Leu Giu Asp Giu Lys Arg Leu Ala His Pro Phe Ser Leu 1847 GCC GTC TTT GAG GAC AAA GTA TTT TGG ACA GAT ATC ATC AAC GAA 612≯Ala Vai Phe Glu Asp Lys Vai Phe Trp Thr Asp lle lie Asn Glu 1892 GCC ATT TTC AGT GCC AAC CGC CTC ACA GGT TCC GAT GTC AAC TTG 627 Ala lie Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp Val Asn Leu 1937 TTG GCT GAA AAC CTA CTG TCC CCA GAG GAT ATG GTC CTC TTC CAC 642 Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu Phe His 1982 AAC CTC ACC CAG CCA AGA GGA GTG AAC TGG TGT GAG AGG ACC ACC 657≯Asn Leu Thr Gin Pro Arg Gly Val Asn Trp Cys Glu Arg Thr Thr 2027 CTG AGC AAT GGC GGC TGC CAG TAT CTG TGC CTC CCT GCC CCG CAG 672 Leu Ser Asn Gly Gly Cys Gin Tyr Leu Cys Leu Pro Ala Pro Gin 2072 ATC AAC CCC CAC TCG CCC AAG TTT ACC TGC GCC TGC CCG GAC GGC 687 ► Ile Asn Pro His Ser Pro Lys Phe Thr Cys Ala Cys Pro Asp Gly 2117 ATG CTG CTG GCC AGG GAC ATG AGG AGC TGC CTC ACA GAG GCT GAG 702 Met Leu Leu Ala Arg Asp Met Arg Ser Cys Leu Thr Glu Ala Glu 2162 GCT GCA GTG GCC ACC CAG GAG ACA TCC ACC GTC AGG CTA AAG GTC 717 Ala Ala Val Ala Thr Gin Glu Thr Ser Thr Val Arg Leu Lys Val 2207 GTC CCT GAT AAA ACT GTG AGA TGG TGT GCA GTG TCG GAG CAT GAG 732 Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu His Glu

FIGURE 5C

2252 GCC ACT AAG 1 CAG AGT TTC CGC GAC CAT ALL AAA AGC GTC ATT 747 Ala Thr Lys Cys Gin Ser Phe Arg Asp His Met Lys Ser Val IIe 2297 CCA TCC GAT GGT CCC AGT GTT GCT TGT GTG AAG AAA GCC TCC TAC 762 Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr 2342 CTT GAT TGC ATC AGG GCC ATT GCG GCA AAC GAA GCG GAT GCT GTG 777 Leu Asp Cys lle Arg Ala lle Ala Ala Asn Glu Ala Asp Ala Val 2387 ACA CTG GAT GCA GGT TTG GTG TAT GAT GCT TAC TTG GCT CCC AAT 792 Thr Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn 2432 AAC CTG AAG CCT GTG GTG GCA GAG TTC TAT GGG TCA AAA GAG GAT 807 Asn Leu Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp 2477 CCA CAG ACT TIC TAT TAT GCT GTT GCT GTG GTG AAG AAG GAT AGT 822 Pro Gin Thr Phe Tyr Tyr Ala Vai Ala Vai Vai Lys Lys Asp Ser 2522 GGC TTC CAG ATG AAC CAG CTT CGA GGC AAG AAG TCC TGC CAC ACG 837 Gly Phe Gin Met Asn Gin Leu Arg Gly Lys Lys Ser Cys His Thr 2567 GGT CTA GGC AGG TCC GCT GGG TGG AAC ATC CCC ATA GGC TTA CTT 852 Gly Leu Gly Arg Ser Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu 2612 TAC TGT GAC TTA CCT GAG CCA CGT AAA CCT CTT GAG AAA GCA GTG 867 Tyr Cys Asp Leu Pro Glu Pro Arg Lys Pro Leu Glu Lys Ala Val 2657 GCC AAT TTC TTC TCG GGC AGC TGT GCC CCT TGT GCG GAT GGG ACG 882 Ala Asn Phe Phe Ser Gly Ser Cys Ala Pro Cys Ala Asp Gly Thr 2702 GAC TTC CCC CAG CTG TGT CAA CTG TGT CCA GGG TGT GGC TGC TCC 897 Asp Phe Pro Gin Leu Cys Gin Leu Cys Pro Gly Cys Gly Cys Ser 2747 ACC CTT AAC CAA TAC TTC GGC TAC TCG GGA GCC TTC AAG TGT CTG 912 Thr Leu Asn Gin Tyr Phe Gly Tyr Ser Gly Ala Phe Lys Cys Leu 2792 AAG GAT GGT GCT GGG GAT GTG GCC TTT GTC AAG CAC TCG ACT ATA 927 Lys Asp Gly Ala Gly Asp Val Ala Phe Val Lys His Ser Thr ile 2837 TTT GAG AAC TTG GCA AAC AAG GCT GAC AGG GAC CAG TAT GAG CTG 942) Phe Glu Asn Leu Ala Asn Lys Ala Asp Arg Asp Gin Tyr Giu Leu 2882 CTT TGC CTA GAC AAC ACC CGG AAG CCG GTA GAT GAA TAC AAG GAC 957 Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp Glu Tyr Lys Asp 2927 TGC CAC TTG GCC CAG GTC CCT TCT CAT ACC GTC GTG GCC CGA AGT 972 Cys His Leu Ala Gin Val Pro Ser His Thr Val Val Ala Arg Ser 2972 ATG GGC GGC AAG GAG GAC TTG ATC TGG GAG CTT CTC AAC CAG GCC 987 Met Gly Gly Lys Glu Asp Leu !le Trp Glu Leu Leu Asn Gln Ala

3017 CAG GAA CAT T1 GGC AAA GAC AAA TCA AAA GAA TTC CAA CTA TTC 1002 GIn Glu His Phe Gly Lys Asp Lys Ser Lys Glu Phe Gin Leu Phe 3062 AGC TCT CCT CAT GGG AAG GAC CTG CTG TTT AAG GAC TCT GCC CAC 1017 Ser Ser Pro His Gly Lys Asp Leu Leu Phe Lys Asp Ser Ala His 3107 GGG TTT TTA AAA GTC CCC CCA AGG ATG GAT GCC AAG ATG TAC CTG 1032 Gly Phe Leu Lys Val Pro Pro Arg Met Asp Ala Lys Met Tyr Leu 3152 GGC TAT GAG TAT GTC ACT GCC ATC CGG AAT CTA CGG GAA GGC ACA 1047 Gly Tyr Glu Tyr Val Thr Ala lle Arg Asn Leu Arg Glu Gly Thr 3197 TGC CCA GAA GCC CCA ACA GAT GAA TGC AAG CCT GTG AAG TGG TGT 1062 Cys Pro Glu Ala Pro Thr Asp Glu Cys Lys Pro Vai Lys Trp Cys 3242 GCG CTG AGC CAC CAC GAG AGG CTC AAG TGT GAT GAG TGG AGT GTT 1077 Ala Leu Ser His His Glu Arg Leu Lys Cys Asp Glu Trp Ser Val 3287 AAC AGT GTA GGG AAA ATA GAG TGT GTA TCA GCA GAG ACC ACC GAA 1092 Asn Ser Val Gly Lys IIe Glu Cys Val Ser Ala Glu Thr Thr Glu 3332 GAC TGC ATC GCC AAG ATC ATG AAT GGA GAA GCT GAT GCC ATG AGC 1107 Asp Cys IIe Ala Lys IIe Met Asn Gly Glu Ala Asp Ala Met Ser 3377 TTG GAT GGA GGG TTT GTC TAC ATA GCG GGC AAG TGT GGT CTG GTG 1122 Leu Asp Gly Gly Phe Val Tyr IIe Ala Gly Lys Cys Gly Leu Val 3422 CCT GTC TTG GCA GAA AAC TAC AAT AAG AGC GAT AAT TGT GAG GAT 1137 Pro Val Leu Ala Glu Asn Tyr Asn Lys Ser Asp Asn Cys Glu Asp 3467 ACA CCA GAG GCA GGG TAT TTT GCT GTA GCA GTG GTG AAG AAA TCA 1152 Thr Pro Glu Ala Gly Tyr Phe Ala Val Ala Val Val Lys Lys Ser 3512 GCT TCT GAC CTC ACC TGG GAC AAT CTG AAA GGC AAG AAG TCC TGC 1167 Ala Ser Asp Leu Thr Trp Asp Asn Leu Lys Gly Lys Lys Ser Cys 3557 CAT ACG GCA GTT GGC AGA ACC GCT GGC TGG AAC ATC CCC ATG GGC 1182 His Thr Ala Vai Gly Arg Thr Ala Gly Trp Asn ile Pro Met Gly 3602 <u>CTG CTC TAC AAT AAG ATC AAC CAC TGC AGA TTT GAT GAA TTT TTC</u> 1197 Leu Leu Tyr Asn Lys IIe Asn His Cys Arg Phe Asp Glu Phe Phe 3647 AGT GAA GGT TGT GCC CCT GGG TCT AAG AAA GAC TCC AGT CTC TGT 1212 ▶ Ser Giu Giy Cys Ala Pro Giy Ser Lys Lys Asp Ser Ser Leu Cys 3692 AAG CTG TGT ATG GGC TCA GGC CTA AAC CTG TGT GAA CCC AAC AAC 1227 Lys Leu Cys Met Gly Ser Gly Leu Asn Leu Cys Glu Pro Asn Asn 3737 AAA GAG GGA TAC TAC GGC TAC ACA GGC GCT TTC AGG TGT CTG GTT 1242 Lys Glu Gly Tyr Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Val

FIGURE 5E

3782 GAG AAG GGA C GTG GCC TTT GTG AAA CAC C... ACT GTC CCA CAG 1257 GIU Lys Gly Asp Val Ala Phe Val Lys His Gin Thr Val Pro Gin 3827 AAC ACT GGG GGA AAA AAC CCT GAT CCA TGG GCT AAG AAT CTG AAT 1272 Asn Thr Gly Gly Lys Asn Pro Asp Pro Trp Ala Lys Asn Leu Asn 3872 GAA AAA GAC TAT GAG TTG CTG TGC CTT GAT GGT ACC AGG AAA CCT 1287 Glu Lys Asp Tyr Glu Leu Leu Cys Leu Asp Gly Thr Arg Lys Pro 3917 GTG GAG GAG TAT GCG AAC TGC CAC CTG GCC AGA GCC CCG AAT CAC 1302 Val Glu Glu Tyr Ala Asn Cys His Leu Ala Arg Ala Pro Asn His 3962 GCT GTG GTC ACA CGG AAA GAT AAG GAA GCT TGC GTC CAC AAG ATA 1317 Ala Val Val Thr Arg Lys Asp Lys Glu Ala Cys Val His Lys Ile 4007 TTA CGT CAA CAG CAG CAC CTA TTT GGA AGC AAC GTA ACT GAC TGC 1332 Leu Arg Gin Gin His Leu Phe Gly Ser Asn Val Thr Asp Cys 4052 TCG GGC AAC TIT TGT TTG TTC CGG TCG GAA ACC AAG GAC CIT CTG 1347 Ser Gly Asn Phe Cys Leu Phe Arg Ser Glu Thr Lys Asp Leu Leu 4097 TTC AGA GAT GAC ACA GTA TGT TTG GCC AAA CTT CAT GAC AGA AAC 1362 Phe Arg Asp Asp Thr Val Cys Leu Ala Lys Leu His Asp Arg Asn 4142 ACA TAT GAA AAA TAC TTA GGA GAA GAA TAT GTC AAG GCT GTT GGT 1377 Thr Tyr Glu Lys Tyr Leu Giy Glu Glu Tyr Val Lys Ala Val Gly 4187 AAC CTG AGA AAA TGC TCC ACC TCA TCA CTC CTG GAA GCC TGC ACT 1392 \blacktriangleright Asn Leu Arg Lys Cys Ser Thr Ser Ser Leu Leu Glu Ala Cys Thr 4232 TTC CGT AGA CCT TAAAATCTCAGAGGTAGGGCTGCCACCAAGGTGAAGATGGGAAC 1407 Phe Arg Arg Pro ••• 4288 GCAGATGATCCATGAGTTTGCCCTGGTTTCACTGGCCCAAGTGGTTTGTGCTAACCACGT 4348 CTGTCTTCACAGCTCTGTGTTGCCATGTGTGCTGAACAAAAAATAAAAATTATTATTGAT 4408 TTTATATTTCGGGGGGGGGGGCCCCTAGACCTGAGGGTCCCCACCTGGGACCCTT 4468 GAGAGTATCAGGTCTCCCACGTGGGAGACAAGAAATCCCTGTTTAATATTTTAAACAGCAG 4528 TGTTCCCCATCTGGGTCCTTGCACCCCTCACTCTGGCCTCAGCCGACTGCACAGCGGCCC 4588 CTGCATCCCCTCTAGA

FIGURE 5F

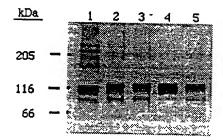


FIGURE 6

.-.<u>ش</u>.-.

Specific Binding of Human LDL to LDLR/TF Chimeric Protein

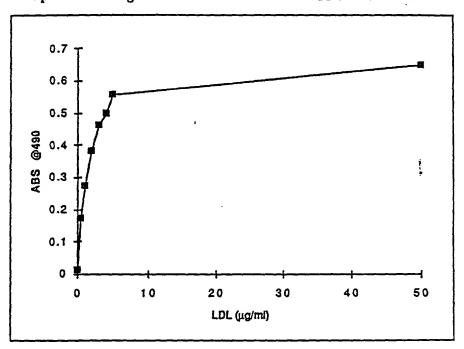


FIGURE 7

Chimeric Protein Binding to LDL is Sensitive to EDTA and pH

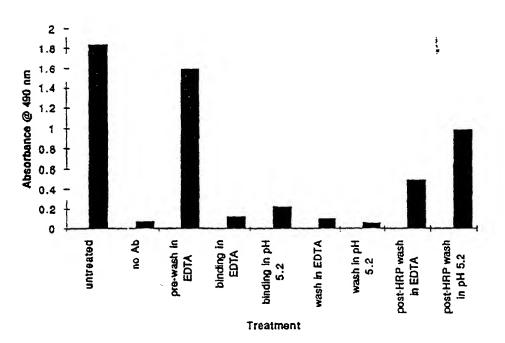


FIGURE 8

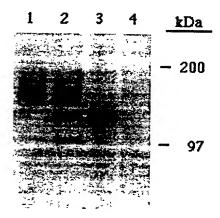


FIGURE 9